Relationship Between the Postoperative Delirium and Dementia in Elderly Surgical Patients: Alzheimer's Disease or Vascular Dementia Relevant Study

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Abstract

Background: Delirium is common in elderly surgical patients and the etiologies of delirium are multifactorial. Dementia is an important risk factor for delirium. This study was conducted to investigate the clinical relevance of surgery to the dementia in Alzheimer's disease (AD) or Vascular dementia (VaD).

Methods and Findings: From March 2018 to April 2019, 95 patients, aged ≥56 years and undergoing surgery were retrospectively enrolled. Multivariate analysis was performed for risk factors that showed a significant difference between delirium and non delirium groups. First, we reviewed 29 patients with previous diagnosed dementia and 66 healthy controls, and the differences in postoperative delirium (POD) between these groups were examined. Second, the patients with dementia were classified into 2 groups: AD and VaD. VaD is a heterogeneous disease, which included poststroke VaD, subcortical VaD, and combined VaD (AD + VaD). Finally, this study evaluated risk factors for POD in underlying medical conditions and c-reactive protein (CRP) level.

Among 95 surgical patients with a mean age of 77.05 years, 41 (43.2%) developed POD. The frequency of POD was higher in dementia patients compared to non dementia groups {82.80% *vs.* 25.80%; odds ratio (OR) 13.34; [95% confidence interval (CI) 3.99–44.66]; P<0.05}. Of the 41 POD patients, twenty-four were diagnosed dementia. In this study, total 29 dementia patients were divided into two groups based on AD (n = 19) or VaD (n = 9). One Parkinson's disease (PD) with dementia was diagnosed delirium and the PD dementia (PDD) patient has been excluded. Among, twenty-three dementia patients with delirium, there were 16 of AD (84.20%) and 7 of VaD (77.80%). There was no significant difference in POD between AD and VaD. Of the risk factors, age {(OR) = 0.14; [(CI) 1.03 − 1.25]; P<0.05} was independently associated with POD in patients undergoing surgery. Prevalence of delirium was not correlated with conditions, such as hypertension (HTN), diabetes mellitus (DM),

gender and CRP value {HTN, 42.90% *vs.* 43.60%: DM, 45.50% *vs.* 33.30%: female, 27.2% of 63.0 *vs.* male 13.8% of 32.0}.

Conclusion: Dementia play a key role in the predisposing factor of POD in elderly patients, but found no clinical difference between two subgroups. It is estimated that AD and VaD would share the pathophysiology, two subtype dementia consequently makes a similar contribution to delirium incidence rates in elderly postoperative patients. The results of our study may contribute to reduce POD occurs through potentially vulnerable patients care.

Keywords: Delirium, Risk factors, Dementia, Relevant study, Pathophysiology

Introduction

Delirium is undisclosed syndrome in the elderly patients after a major operation. Multiple risk factors for the development of POD in old age patients include age, underline disease, type of surgery, depressed mood and severity of medical illness. It has been referred that delirium presentation is typically 24-72 hours after the completion of a surgical procedure. For example, POD following spine surgery has been reported to occur in 24.3% (17/70) of elderly patients. The incidence of delirium following orthopedic surgery has been reported to be 4-65%. For example, POD has been reported 35-65% in patients undergoing operation of a hip fracture. It is dependent on the type of surgery.

AD is the most common subtype, accounting for 60-80% of dementia patients and VaD is second most common form. The recent paper showed that delirium or dementia-related pathology doubled the rate of cognitive decline. These results supported the hypothesis that delirium and dementia have intercorrelation and synergistic effects on cognitive decline. The recognition and treatment of delirium is important to clinician. POD is associated with poor outcomes including functional decline, longer hospitalization, greater costs, and higher mortality. One of our aims was to accentuate previous

findings that the incidence of POD is increased in elderly surgical patients who have a clinical diagnosis of dementia. However, main purpose of this study was to conduct the analysis of POD patients according to dementia subtype (AD and VaD) enrolled in the hospital. In addition to hypothesis, we exam that the association between POD and risk factors has been interacted by age, gender, underline disease and inflammation CRP level.

Materials and Methods

Study design

The local ethics committee approved this study, and each patient provided written informed consent for participation. All subjects aged 56 years and older who were admitted for orthopaedic and spinal surgery during the period from March 2018 to April 2019 screened for this study. During 14 months period, a total of 95 patients were enrolled with a mean age of 77.05 ± 6.70 years (range 56 - 92). The inclusion criteria were the following: patients of ago ≥ 56years old [1], who were scheduled to undergo orthopaedic and spinal surgery [2], Type of surgery included mainly discectomy, laminectomy, fusion and instrumented fusion, total knee arthroplasty, other elective knee surgery, elective total hip arthroplasty ([total hip replacement] / bipolar hemiarthroplasty, revision hip surgery, open reduction and internal fixation [ORIF] / arthroplasty for hip fracture) [3], Risk factors of delirium were evaluated for dementia, age, sex, HTN, DM and CRP level [4]. The patients with previous diagnosed dementia were classified into 2 groups: AD and VaD [(poststroke VaD, subcortical VaD, and combined VaD (AD + VaD)] [5], And we also included patients with history of use of acetylcholinesterase inhibitors, such as donepezil, galantamine or rivstigmine [6]. Surgical patients allocated to receive general anesthesia, regional anesthesia (spinal or epidural) or brachial plexus block.

In this study, the AD patients met the Diagnostic and Statistical Manual of Mental Disorders, 4 thedition (DSM-IV) criteria and VaD patients who assessed brain images were included with presence of cerebrovascular diseases. Serum CRP levels were routinely measured in all surgical patients and healthy controls. Individual characteristics and clinical data were obtained from patient interviews, caregiver statements and medical records. Patients with POD were assigned to a delirium group, while patients without delirium were enrolled in the control group. Patients were screened for delirium daily by the primary care nurses in the wards after surgery using the Confusion Assessment Method (CAM). The short CAM consists of scoring derived from the following 4 clinical assessment protocols : (I) determine the presence of an acute mental change from baseline behavior and if present, the nature of this behavior's fluctuation course (mental status changes from hours to days); (II) determine if the patient is inattentive, easily distracted, or unable to participate in an interview; (III) evaluate the presence of disorganized thought, pressured speech or tangential speech; (IV) assess the patient's level of consciousness. A diagnosis of POD requires the presence of features 1 and 2 accompanied by either feature 3 or 4.

Statistical analysis

Data are presented as the mean ± standard deviation (SD). A χ^2 test, and multivariate logistic regression analysis were used for statistical analysis. All variables with a significance level of $p < 0.05$ in the univariate analysis were included as independent variables in a forward stepwise regression method for the multivariate analysis. A value of $p < 0.05$ was considered statistically significant.

Results

Of the participants enrolled in the Seoul Chuk Hospital from March 01, 2018 to April 30, 2019, 95 underwent a surgical procedure requiring anesthesia. Ninety-five patients underwent orthopaedic and spinal surgeries were enrolled in this study, POD occurred in 41 patients (43.2 %). The 41 delirium patients were diagnosed within seven days after surgery. As compared to the control group, there was a higher prevalence of POD in dementia group. Of the 41 POD patients, twenty-four were previously diagnosed dementia. In the statistical analysis, we found that within the delirium group, 24 patients were dementia and 17 patients were not previous dementia {82.80% vs. 25.80%; odds ratio (OR) 13.34; [95% confidence interval (CI) 3.99–44.66]; P<0.05}. The average age of the patients in delirium group was 77.05 ± 6.70 years (ranging from 56 to 92 years), and the delirious group was consist of 14 males and 27 females.

In this study, total 29 dementia patients were divided into two groups based on AD (n = 19) or VaD (n = 9). One Parkinson's disease (PD) with dementia was diagnosed delirium and the PDD patient has been excluded. Among, twenty-three dementia patients with delirium, there were 16 of AD (84.20%) and 7 of VaD (77.80%). There was no significant difference in POD incidence rate between AD and VaD patients **(Table 1)**.

The mean age of the delirium positive group was significantly higher than that of the delirium negative group {(OR) = 0.14; [(CI) 1.03–1.25]; P<0.05}. In the present study, older age was associated with a higher incidence of postoperative delirium. Subsequently, multivariate logistic regression analysis was performed for other risk factors. Postoperative CRP level, type of surgery and anesthesia, gender and underline disease were analyzed. However, there was no significant difference in comorbidities HTN, DM, sex and CRP value. The results of the logistic regression analysis for identifying the risk factors for POD are summarized in **Table 2**.

Discussion

This retrospective study investigated the effects of dementia subtype on POD in patients who underwent orthopaedic or spinal surgery and examined the interrelationship between multivariate risk factors analysis and POD. This study confirmed that dementia is associated with a 13.34 fold increase in prevalence of POD. Moreover, the greater influence of delirium may reflect the older age in this

study. In particular, this is the first study to evaluate the hypothesis that dementia is a risk factor for delirium but dementia subtype (AD or VaD) is no significant difference in incidence of POD.

Table 1: The prevalence of delirium in each type of dementia. A total 41 participants (43.2 %) experienced delirium within postoperative 7 hospital days. Of these, 23 patients were diagnosed as previous dementia. Among, twenty-three dementia patients with delirium, there were 16 of AD (84.20%) and 7 of VaD (77.80%) and significant difference in POD incidence rate between AD and VaD patients.

Variable	Non-delirium group	Delirium group	χ2 (p)
Non-dementia group	49(74.2)	17(25.8)	
Dementia group	5(17.2)	24(82.8)	
AD	3(15.8)	16(84.2)	
PDD	0(0.0)	1(100.0)	26.684*** 0
VD	2(22.2)	7(77.8)	
***p<.001			
Values are presented as number (%).			
*Calculated by chi-sqaure test.			

Table 2: Multivariable logistic regression analysis of the predicted effect of delirium. The results of risk factors for delirium is adjusted by age, sex and co-morbidity, given with 95% CIs [lower confidence interval, upper confidence interval.

Variable	p-value	Odds ratio	95% confidence interval of Exp (B)	
			Lower	Upper
Age	0.01	1.136	1.031	1.251
Gender	0.41	0.602	0.18	2.017
Dementia	0	13.342	3.985	44.663
HTN	0.25	2.099	0.587	7.509
DM	0.29	0.451	0.104	1.967
CRP	0.49	1.027	0.952	1.107

At least two thirds of cases of delirium occur in patients with underlying dementia or cognitive impairment, suggesting that the underlying vulnerability of the brain in dementia predisposes surgical patients to the development of delirium when exposed to precipitating factors such as medical illnesses, infections, medications, and medical procedures. Previous studies have postulated shared underlying mechanisms, as both delirium and dementia have been shown to be associated with decreased cerebral oxidative metabolism, cholinergic deficiency and inflammation. In addition, neuroimaging studies have documented regions of hypoperfusion in patients with delirium, suggesting that delirium may incite a derangement in brain vascular function that may lead to dementia in some cases.

There are several reasons why dementia subtypes (AD or VaD) contribution to delirium is similar. AD is a neurodegenerative disorder and vascular disorders are important features in chronic neurodegeneration in AD. Therefore, neurovascular dysfunction could have a major role in the pathogenesis of AD. The association between circle of Willis atherosclerosis and AD-type pathology provides further evidence that vascular disease and AD are interrelated and suggests that common etiologic or reciprocally synergetic pathophysiological mechanisms promote both pathologies. For example, recent papers indicate an overlap between AD and post-stroke dementia (PSD), which seems to share risk factors and neuropathology. In most population samples these two disorders appear together, and the consensus is growing that a degenerative component has a more important role in determining PSD onset shortly after stroke than previously recognized.

There is an increasing evidence that cerebrovascular dysfunction plays a role not only in vascular causes of cognitive alterations but also in AD. Cognitively patients, with AD, show sometimes mixed degrees of associated vascular lesions in 30-60% of AD cases. In opposition, AD pathology may be present in 40%-80% of VaD patients.

The results of these current studies not only confirm the need to identify patients at risk factors for postoperative delirium, but also investigate the highly interactive nature of dementia (AD or VaD) and delirium. Finally, it is estimated that AD and VaD would share the pathophysiology, two subtype dementia (AD *vs.* VaD) consequently makes a similar contribution to delirium incidence rates in elderly surgical patients.

There are multiple risk factors for the development of POD in old age patients. For instance, anesthesia contributes to well-described mechanisms of Alzheimer's neuro-pathogenesis and provides the first demonstration of a potential pathogenic link between delirium and the more long-term sequelae of dementia. Interrelationship of POD and risk factors (e.g. gender underline disease and CRP level) have not yet clearly demonstrated.

Conclusion

This study has several strengths and limitation. It is the first study to provide statistical analysis and interpretation of data for potential impact of dementia subtypes on POD. Early identification of patients with baseline cognitive impairment and dementia to prevent delirium could reflect good surgical outcomes and shorten hospital stay. However, we were limited by the retrospective study and our hospital patient. To clarify the relationship of cognitive impairment and delirium in the pathogenesis, future longitudinal studies involving a large cohort are required.

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